

CLAIMS

1. A recombinant DNA sequence which encodes the complete amino acid sequence of a glutamine synthetase (GS).
2. The recombinant DNA sequence of claim 1, which encodes the complete amino acid sequence of an eukaryotic GS.
3. The recombinant DNA sequence of claim 2, which encodes the complete amino acid sequence of a mammalian GS.
4. The recombinant DNA sequence of claim 3, which encodes the complete amino acid sequence of a rodent GS.
5. The recombinant DNA sequence of claim 4, which encodes the complete amino acid sequence of a hamster GS.
6. The recombinant DNA sequence of claim 5, which comprises the amino acid coding portion of the sequence shown in Figure 2.
7. The recombinant DNA sequence shown in Figure 2.
8. A recombinant DNA sequence from one species which hybridises under high stringency conditions with the recombinant DNA sequence of ~~any one of~~ ^{claim 1} claims 1 to 6 or a part thereof from a different species.
9. The recombinant DNA sequence of ~~any one of~~ ^{claim 1} claims 1 to 8, which is cDNA.
10. The recombinant DNA sequence of claim 9 wherein the cDNA is derived by reverse transcription.
11. The recombinant DNA sequence of ~~any one of~~ ^{claim 1} claims 1 to 10, which comprises a fragment of genomic DNA.
12. Use of the recombinant DNA sequence of ~~any~~ ^{claim 1} one of claims 1 to 6 or any fragment thereof as a hybridisation probe.

26. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS, which comprises co-transforming a host cell with a vector according to claim 15, ~~claim 18 or claim 19 when dependent on claim 15, or any one of claims 20 to 27~~, and a vector comprising said desired protein recombinant DNA sequence.

27. A method for co-amplifying a recombinant DNA sequence which encodes the complete amino acid sequence of a desired protein other than GS which comprises transforming a host cell with a vector according to claim 17, ~~claim 18 or claim 19 when dependent on claim 17, claim 23 or claim 24~~.

28. The method of ~~claim 26 or claim 27~~, wherein the desired protein is tissue plasminogen activator.

29. The method of ~~any one of claims 26 to 28~~, ^{claim 26} wherein amplification is achieved by selection for resistance to progressively increased levels of a GS inhibitor.

30. The method of claim 29, wherein the GS inhibitor is phosphinothricin or methionine sulphoxime.

31. The method of claim 29 ~~or claim 30~~, wherein after amplification, the level of GS accumulation is reduced by adding glutamine to the culture medium.

32. The method of ~~any one of claims 29 to 31~~, wherein the amount of GS inhibitor required

-41-

to cause amplification is reduced by the addition of methionine to the culture medium.

33. The method of ~~any one of claims 26 to 30 when dependent on claim 18 or claim 19~~, wherein the GS-encoding recombinant DNA sequence expression is switched on during selection and amplification and subsequently down-regulated.

34. Use of a vector according to ~~any one of claims 15 and 17 to 24~~ as a dominant selectable marker by transforming a host cell which contains an active GS gene with the vector, thereby conferring transformant cells with resistance to GS inhibitors.

35. Use of a vector according to ~~any one of claims 15 and 17 to 24~~ in endowing a cell line with the ability to survive in a medium lacking glutamine by transforming a host cell either completely lacking or reduced in GS activity with the vector.

36. The method of ~~any one of claims 26 to 34~~, wherein the host cell is a mammalian cell.

37. The method of ~~any one of claims 26 to 34~~, wherein the host cell is a CHO-KI cell.

38. The method of claim 35, wherein the host cell is a myeloma cell.

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